

M. A. Persinger · B. E. McKay · C. A. O'Donovan ·
S. A. Koren

Sudden death in epileptic rats exposed to nocturnal magnetic fields that simulate the shape and the intensity of sudden changes in geomagnetic activity: an experiment in response to Schnabel, Beblo and May

Received: 6 August 2003 / Revised: 9 July 2004 / Accepted: 1 October 2004 / Published online: 16 November 2004
© ISB 2004

Abstract To test the hypothesis that sudden unexplained death (SUD) in some epileptic patients is related to geomagnetic activity we exposed rats in which limbic epilepsy had been induced to experimentally produced magnetic fields designed to simulate sudden storm commencements (SSCs). Prior studies with rats had shown that sudden death in groups of rats in which epilepsy had been induced months earlier was associated with the occurrence of SSCs and increased geomagnetic activity during the previous night. Schnabel et al. [(2000) *Neurology* 54:903–908] found no relationship between SUD in human patients and geomagnetic activity. A total of 96 rats were exposed to either 500, 50, 10–40 nT or sham (less than 10 nT) magnetic fields for 6 min every hour between midnight and 0800 hours (local time) for three successive nights. The shape of the complex, amplitude-modulated magnetic fields simulated the shape and structure of an average SSC. The rats were then seized with lithium and pilocarpine and the mortality was monitored. Whereas 10% of the rats that had been exposed to the sham field died within 24 h, 60% of the rats that had been exposed to the experimental magnetic fields simulating natural geomagnetic activity died ($P<.001$) during this period. These results suggest that correlational analyses between SUD in epileptic patients and increased

geomagnetic activity can be simulated experimentally in epileptic rats and that potential mechanisms might be testable directly.

Keywords: Sudden death · Epilepsy · Sudden storm commencement · Geomagnetic activity

The risk of sudden unexpected death (SUD) in subpopulations of epileptic patients has been reported to be between 10 and 20 times greater than the normal population (Leestma et al. 1989). The etiology of this enhanced mortality has been attributed to factors that range from cessation of normal cardiac functions during the extreme physiology associated with tonic-clonic convulsions (Terrance 1990), to temporal discrepancies in the phasic activity of descending neuropathways from the insula and the amygdala directly to and through the medullary parasolitary nuclei en route to the atria (Oppenheimer et al. 1991; Persinger 1995a, b).

Increased periods of global geomagnetic activity (when daily averages exceed 20 or 30 nT) have been associated with increased rates of convulsions in temporal lobe epileptics (Rajaram and Mitra 1981) and more frequent episodes of overt Racine level 6 forelimb clonus in rats (Racine 1972) in which limbic epilepsy had been previously induced by a systemic injection of lithium and pilocarpine (Persinger et al. 1993; Bureau and Persinger 1995; Persinger 1995a, b). Comparable enhancements in the numbers of overt seizures in chronically epileptic rats occurred when they were exposed in their home cages to experimentally generated magnetic fields with progressively increasing and decreasing step-like changes in intensity between 10 and 50 nT. Each step was 30 s and the total cycle was 3 min (5.5 mHz). The pattern was designed to imitate the temporal structures of natural conditions (Michon and Persinger 1997).

While monitoring the status and behavior of approximately 150 rats in which limbic epilepsy had been in-

M. A. Persinger (✉) · S. A. Koren
Behavioral Neuroscience Laboratory,
Laurentian University, Sudbury, Ontario, P3E 2C6, Canada
e-mail: mpersinger@laurentian.ca
Fax: +1-705-6713844

B. E. McKay
Neuroscience Research Group,
University of Calgary, Calgary, Alberta, T2N 4N1, Canada

C. A. O'Donovan
EEG and Evoked Potentials Laboratory,
Sections of Epilepsy and Stroke,
Department of Neurology, Wake Forest University,
Medical Center Boulevard,
Winston-Salem, NC 27157, USA

duced by lithium and pilocarpine, Persinger (1995a, b) noted that sudden death occurred in 11 such rats. Most ($n=9$) of these deaths occurred during local night when there had been a sudden storm commencement (SSC) in the Earth's magnetic field and the subsequent averaged 24-h global geomagnetic activity had exceeded about 40 nT. These results have been replicated subsequently and similar patterns were found more recently for a population of human epileptics by Stoupe et al. (2002). However, the analyses by Schnabel et al. (2000) of 46 epileptic patients with definite SUD and 108 epileptic patients with known causes of death did not support this association.

There are several possible explanations for these discrepancies, which might include methods of analyses, employment of appropriate indices of geomagnetic activity, and the criteria for patient selection. Because all of the studies associating sudden cardiac death in rats and humans with increases in geomagnetic activity mentioned have been correlational, the possibility of third factors or confounding factors that spuriously generated the correlations must be considered. The only test of the validity of a correlational relationship is the experiment.

We hypothesized that the rates of change in the intensities, and the patterns sequestered within temporal patterns of geomagnetic activity (the equivalent of a "time fractal"), are the critical factors for sudden death during epileptic seizures. The concept would be similar to the assumption in pharmacology where the physical structure of the molecule and the dose rate (dosing schedule) per se determine the effect upon the organism. For magnetic fields, the temporal pattern of the applied variations in intensity may contain the biologically relevant properties (Persinger 2003). To test this hypothesis, we exposed rats during three successive nights to designed magnetic fields whose temporal characteristics imitated the rise times of SSCs. During the last 100 years, the rise times for most SSCs have been about 5 or 6 min. The median values for the changes in intensity of the most active component of the geomagnetic field have been between 15 and 50 nT (Mayaud 1975).

We selected nocturnal exposures because of the preferential effect of experimental and natural magnetic fields on nocturnal melatonin (Burch et al. 1999; Lerchl et al. 1991; Reiter 1993; Yaga et al. 1993), the diminished levels of which are related to increased probability of seizure (Costa-Lotufo et al. 2002). Three nights rather than one night was selected in order to enhance what was predicted to be a weak effect to a magnitude sufficient to achieve statistical significance ($P<.01$) with a small sample size. This type of experimental design also reduced the number of rats required to be traumatized by the induction of the epileptic process so that both scientific validity and the guidelines of the Canadian Council for Animal Care could be accommodated.

To create the seizures, we injected rats systemically (sub. cu.) with 3 mEq/kg lithium chloride and then 30 mg/kg pilocarpine (Persinger et al. 1993). This combination induces reliable overt limbic seizures, typified by rearing

and forelimb clonus followed by status epilepticus, that are easily verified by electroencephalography. Most of these rats die within 24 h after induction of seizure unless they are treated within 30 min after the appearance of the overt seizures by drugs such as acepromazine or ketamine (Stewart and Persinger 2001). Death is associated with sudden cardiac cessation that is often preceded by periods of cardiac arrhythmia (Harrigan et al. 1994) in a manner similar to the effects of direct stimulation of the chronotropic portion of the insula with the EKG signals from the rat's own cardiac feedback (Oppenheimer et al. 1991).

Materials and methods

A total of 96 male Wistar albino rats obtained from Charles River (Quebec) were employed as subjects. The mean and standard deviation for their weights were 540 and 83 g. In eight separate blocks of experiments (12 rats per block) over a 9-month period, the subjects were placed in one of four (3 rats/cage) 32 cm $\times$ 32 cm $\times$ 45 cm plastic cages. There was no more than one block per month.

The exposure apparatus has been described elsewhere (Cook et al. 2000). In summary, two of the cages were surrounded completely by Helmholtz coils (each 30 ohm), while the other two cages, immediately below, were not. The long axes of the cages (and the coils) were oriented in a north-south direction. The cages contained wood shavings. Food and water were available ad libitum. The light-dark cycle was 12:12 with lights on at 0800 hours.

After 3 days of habituation to the settings, rats in each of the eight blocks of experiments were exposed eight times per night for 6 min each hour, starting at midnight, to a magnetic pattern designed to imitate geomagnetic activity. Square wave 7 Hz magnetic fields from a function generator were amplitude-modulated through a Commodore computer in 14 sequential steps (see figure in Cook et al. 2000) with the duration of each plateau being 14 s during the first 3 min and 20 s and 7 s during the last 1 min 42 s. These changes within the 6 min duration were equivalent to variations of 140 and 71 mHz, while the onset of the pattern once every hour was equivalent to about 0.3 mHz. These periodicities overlap with the primary range of geomagnetic activity (Bubenik et al. 1983). The "ripple" or "rider" frequency of 7 Hz was selected because of its prominence within the Schumann resonance that has been implicated as a zeitgeber for a variety of biological functions (Cherry 2002) and may be a harmonic mode during cardiac fibrillation.

The strength of the field generated within the coils surrounding the housed rats was 50 nT (peak-to-peak) for some blocks of experiments; the peak strength in the control cages was 10 nT. To control for possible cage position effects, in some blocks the maximum field strengths within the coils were about 500 nT (with a range of 10%: 450–550 nT) and the field strengths in the lower cages were between 10 and 40 nT. All measurements were completed with a Metex 3800 multimeter and a magnetic sensor probe (Electric Field Measurements). The presence of the 6-min episodes of magnetic fields was verified directly once per night and recorded automatically on the computer log.

After two nights of exposure to the conditions, 60 of the rats (five blocks) were injected with 3 mEq/kg lithium chloride and then 24 h later with 30 mg/kg of the muscarinic agent pilocarpine. After three nights of exposure the remaining rats ($n=36$; three blocks) were injected with 3 mEq/kg lithium and then 4 h later with the same dosage of pilocarpine. This meant that, before the injection of the pilocarpine, all rats had been exposed for three nights to the treatments. We employed these two intervals because earlier studies had indicated the numbers of spontaneous seizures throughout the rats' lifetimes and their aggressiveness were related to the 4 h or 24 h latency between lithium and pilocarpine (Persinger 1995a, b). However, because there were no significant differences in mortalities between the groups that received the pilo-

carpine 4 h or 24 h after the lithium, the groups were collapsed for a single analysis.

Analyses of variance were completed for the proportions of deaths per cage per 24 h during each of the 3 days following the induction of seizures as a function of the four intensities: sham (less than 10 nT), 10–40, 50 and 500 nT. Because ambient geomagnetic activity has been shown to affect seizure probability, the daily highest and lowest levels for the planetary A index and the 3 h values for the planetary K (kp) indices for the days after the induction of the seizures were obtained from the Recent solar and geomagnetic data website (<http://www.dxlc.solar/indices.html>). These values were correlated with the proportions of deaths for each block separately. All analyses employed SPSS software on a Vax 2000 computer.

Results

The means and standard errors of the mean for the proportions of rats that died suddenly within each successive 24-h period during the 3 days after the induction of seizures as a function of the intensities to which they were exposed during the 3 days before the seizures were induced are shown in Fig. 1. The only statistically significant differences between treatments (different experimental field strengths) occurred during the first 24 h after induction of seizures.

One-way analysis of variance indicated a statistically significant difference [$F(3,92)=9.45$, $P<.001$; eta-squared =25% of variance] between the groups that had been exposed to the four intensities of the experimental simulation of geomagnetic activity. Polynomial analysis indicated significant linear [$F(1,92)=14.93$, $P<.01$] and quadratic [$F(1,92)=6.57$, $P<.05$] terms. Post hoc analyses (Tukey's, $P<.05$) indicated that the latter was due to greater mortality in the group that had been exposed to the 50 nT variation compared to the sham-field and <40 nT group.

The proportion of rats exposed to the sham fields (in six separate experimental blocks) that died was signifi-

cantly correlated ($r=0.96$) only with the range of the daily low of the planetary A-index ($M=6.0$; $SD=4.6$) during the 24 h period following the induction of seizures. The means and standard deviations (in parentheses) for the A-index for the 1st and 2nd day before the key day (the day the rats were seized) were 7.8 (4.6) and 8.6 (3.8), respectively. These values for the 1st and 2nd days after the key day were 4.3 (2.2) and 4.8 (2.6), respectively.

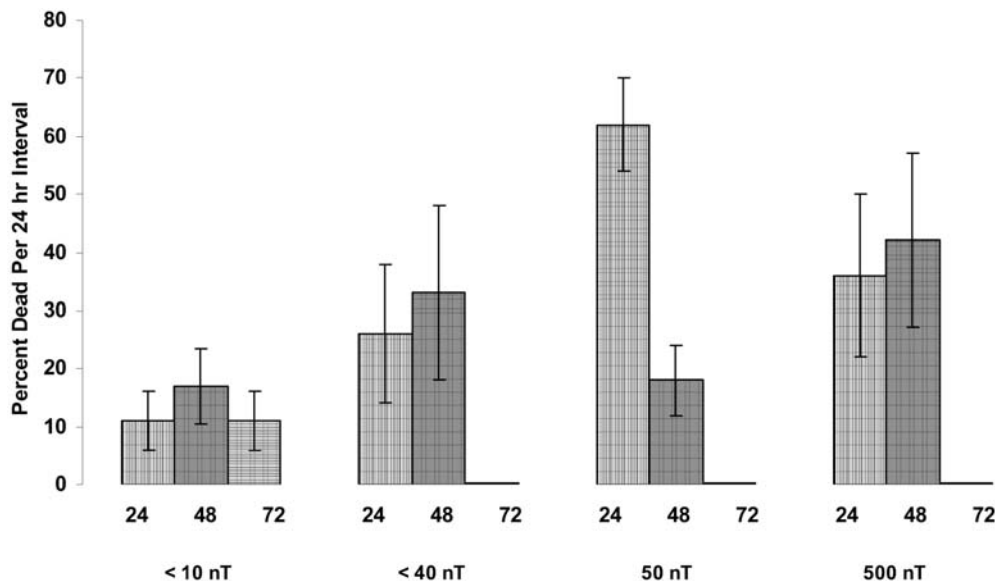
The only statistically significant correlations between the numbers of deaths in the sham field rats and the 3 h kp indices (measured at Boulder, Colo.) occurred during the second (.87), third (.89) and fourth (.91) intervals on the day of the seizures. These periods corresponded to 2200 to 0700 hours that night and the next morning (local time). There were no statistically significant correlations between these geomagnetic indices and the proportions of mortality in groups receiving any of the experimental fields.

Discussion

Over a 2-year period (1988, 1989), Persinger (1995a,b) reported sudden deaths in a population of about 150 rats with chronic epilepsy induced by the single systemic injection of lithium and pilocarpine. Most of these deaths occurred if a sudden geomagnetic impulse, with an amplitude above about 30 nT, had occurred during the previous night.

The results of the present study indicate that a magnetic field designed to imitate natural patterns, presented for 6 min once per hour between midnight and 0800 hours (local time) for three nights, markedly increased the proportion of death in rats if the amplitude was about 50 nT, but not below 10 nT, between 10 and 40 or 500 nT. Most of the deaths occurred within the first 24 h. These results are congruent with the characteristics of the rats that died suddenly in our previous observational study.

Fig. 1 Proportions of sudden death in rats during the three 24 h intervals (24, 48, 72) after induction of seizures, as a function of intensities of the experimentally simulated geomagnetic activity to which the rats had been exposed during the previous three nights



Increased melatonin production (Schapel et al. 1995) has been measured in untreated epileptic patients and clustering of seizures with circadian peaks between 2200 and 0600 hours local time are well known. Increased levels of nocturnal melatonin are induced by consumption of moderately low dosages of ethanol (Myers and Badia 1993) and by sleep deprivation (Badia et al. 1994). Interestingly, common antidepressants such as desimipramine and oral contraceptives such as progestin increase levels of nocturnal melatonin, while common antipsychotic drugs such as clonidine, anxiolytics such as alprazolam, and beta-blockers such as atenolol, decrease melatonin levels (Badia et al. 1994).

The anticonvulsant effects of melatonin in amygdala-kindled rats have been shown (Mevisen and Ebert 1998). Our working hypothesis has been that increases in geomagnetic activity, particularly during local night, diminish the production of circulating melatonin. The decreased concentration of melatonin encourages electrical lability within the hippocampus (Zeiss and Semm 1988) and within specific amygdaloid nuclei.

This sudden disinhibition could promote telencephalic subcortical seizures that result in cardiac dysrhythmias and in sudden death. Lerchl et al. (1991) have found that exposure of rats to pulsed magnetic fields during nocturnal periods depressed the activity of *S-n*-acetyl transferase, the rate-limiting step in the synthesis of melatonin. Consistent with this explanation is the observation by Burch et al. (1999) that increased global geomagnetic activity over 30 nT was associated with reduced nocturnal excretion of a melatonin metabolite in human beings. If less melatonin is synthesized, then less metabolites will be excreted.

However, Schnabel et al. (2000) did not find a statistically significant correlation between daily values for ambient geomagnetic activity and the numbers of daily deaths in epileptic patients who died suddenly or from other sources between the years 1981 and 1992 in Germany. These authors utilized daily global geomagnetic Ap indices on the days of the deaths as well as kp signs at the hour of death and 2 h before death. The sudden unexplained death (SUD) patients were usually younger than those who died from known causes, and were more likely to have died during November or December. The peak in mortality for SUD patients was between 0300 and 0600 hours local time.

One possibility for this discrepancy is that the organization of the rat brain increases its vulnerability to geomagnetic activity. The geometry of the lissencephalic rat brain may promote the more vigorous and pervasive intracortical spread of epileptic seizures than the configuration of the gyrencephalic human brain. If this assumption is valid, then the data for epileptic rats are not generalizable to data for human epileptics.

A second possibility may involve a non-linearity between the intensity of the geomagnetic activity and the physiological processes promoting SUD in epileptic patients. Stoupel et al. (2002) showed that different types of sudden cardiac death in Lithuania between 1994 and 1998

occurred within specific ranges of geomagnetic intensity. In general, the frequencies were higher on days when the amplitude of the geomagnetic activity ranged between about 20 and 70 nT. However, men and women within some age ranges were more likely to die when geomagnetic activity was very quiet.

The assumption that intensity is more important than the temporal structure of the geomagnetic activity may not be valid. The physiological conditions following sudden increases in geomagnetic activity that occur within about 300 s (5 min) may be different qualitatively from the conditions that follow increases in geomagnetic activity that occur within 1,000 s (about 15 min). Several recent studies have indicated that different increments of geomagnetic activity and the complexity of the field may be associated with epileptic-related phenomena (Michon and Persinger 1997; Persinger and Belanger-Cheliew 1999), including sudden infant death (O'Connor and Persinger 1997).

In addition, the effect appears to be transient because successive nightly presentations of geomagnetically simulated fields increase the numbers of spontaneous seizures for only about two or three nights unless there is a change in physiological state (Persinger 1996). Subsequent presentations do not significantly alter seizure probability. About 1 week of no exposure is required before vulnerability to these fields increases again. A similar observation has been reported for the correlations between numbers of spontaneous seizures and geomagnetic activity (Persinger 1995a, b).

One explanation that could accommodate the discrepancies between the results of different researchers involves the temporal structure of SSCs. After the experiments reported here were completed, we obtained a MEDA FM 300 Vector Fluxgate Magnetometer (resolution 1 nT). We carefully measured the intensity of the geomagnetic field when our simulated "sudden impulse" was produced. As shown in Fig. 2, an approximately 15 nT reduction in the intensity of the total (resultant) geomagnetic field (35,000 nT) was suddenly produced during the generation of our 50 nT, 7 Hz, amplitude-modulated experimental field through the horizontal plane of the Helmholtz coils.

Over the last 100 years, only about 10% of SSCs have begun with a sudden reduction in the intensity of the resultant field; 90% have been sudden increases in intensity. The direction of the SSCs [ftp://ftp.ngdc.noaa.gov/STP/SOLAR_DATA/SUDDEN_COMMENCEMENTS/PSTORM/] were obtained for the timepoints at which eight of the nine rats died during the years 1988 and 1989. These "correlational" deaths from the original study (Persinger 1995a, b) formed the basis for the design of the present experiment. Of those original cases, 6 (75%) were associated with a sudden reduction in intensity.

We suggest that, given the presence of the optimal temporal pattern or "frequency", maximum bioeffectiveness may require a critical ratio between the intensity of the changing magnetic fields and the intensity of the steady-state (background) geomagnetic field. In our ex-

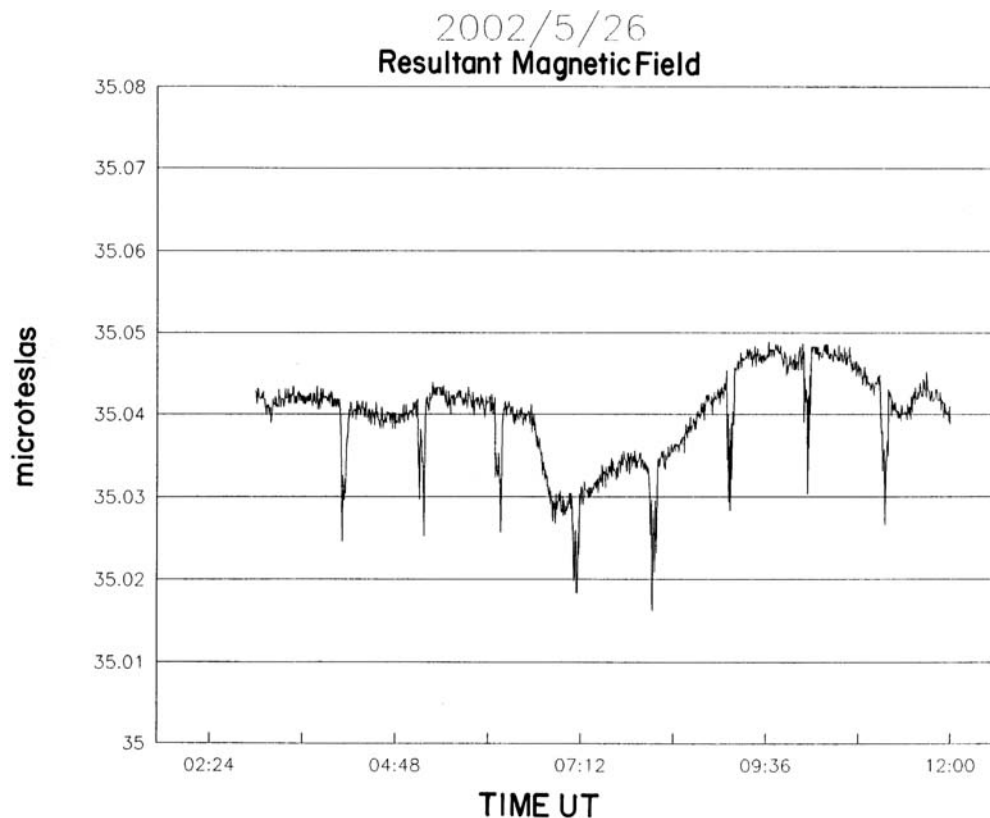


Fig. 2 The shape and intensity of the total geomagnetic field within an exposure coil during a single night. The eight periods associated with the approximately 15 nT reduction in the intensity of the resultant field (about 35,000 nT) represents the activation of the experimentally generated sudden impulse within the horizontal

component (change of about 50 nT). These periods were superimposed upon the natural change in geomagnetic activity during that night as reflected in the decrease (although a slower rate) of about 10 nT around 0630 hours UTC (0230 hours local time)

perimental setting, the resultant strength of the geomagnetic field was about 35,000 nT because of the coils. In other places within the university the resultant intensity ranged from 48,000 to 55,000 nT. If our assumption is valid, then epileptic animals exposed to different areas with different resultant vectors may be most sensitive to different ranges of intensities during geomagnetic storms, or experimental fields that simulate those conditions. However, the values for the changing/steady field ratios would be similar.

Perhaps careful quantification of the specific structure of SSCs and the subsequent geomagnetic activity during the 48–72 h periods around the times of SUD in epileptic patients, particularly those with partial complex (limbic focused) seizures and secondary tonic-clonic convulsions, may resolve the discrepancies between the results of various research groups. The extraction of temporal complexities that contain biological information (Persinger 2003) sufficient to encourage sudden cardiac death would require the cooperation of both the medical neurosciences and the geophysical sciences. Inferences of the biological effectiveness of changes in global geomagnetic activity on the basis of intensity alone may be as limited as inferring the meaning and syntax of a spoken sentence by attending only to its loudness.

Acknowledgements Portions of this research were supported by the Canadian Foundation for the Study of Infant Deaths (SIDs), the Laurentian University Research Fund (LURF), and the Laurentian University Neuroscience Research Group

References

- Badia P, Murphy PJ, Myers BL, Wright KP (1994) Alcohol ingestion and nighttime melatonin levels. *Sleep Res* 23:477
- Bubenik DM, Graf PE, Moore DJ, Ruggles AC, Todd SA (1983) Spectral and coherence properties of geomagnetic fluctuation noise. SRI International: Menlo Park (Contract N00167-81-K-0245)
- Burch JB, Reif JS, Yost MG (1999) Geomagnetic disturbances are associated with reduced nocturnal excretion of a melatonin metabolite in humans. *Neurosci Lett* 266:209–212
- Bureau YRJ, Persinger MA (1995) Decreased latencies for limbic seizures induced in rats by lithium-pilocarpine occur when daily average geomagnetic activity exceeds 20 nT. *Neurosci Lett* 192:142–144
- Cherry N (2002) Schumann resonances, a plausible biophysical mechanism for the human health effects of solar/geomagnetic activity. *Nat Haz* 26:279–331
- Cook LL, Persinger MA, Koren SA (2000) Differential effects of low frequency, low intensity (<6 mG) nocturnal magnetic fields upon infiltration of mononuclear cells and numbers of mast cells in Lewis rats. *Toxicol Lett* 118:9–19

- Costa-Lotufo LV, Fonteles MM, Lima ISP, de Oliveira AA, Nascimento VS, de Bruin VMS, Viana GSB (2002) Attenuating effects of melatonin on pilocarpine-induced seizures in rats. *Comp Biochem Physiol C* 131:521–529
- Harrigan T, Bureau YRJ, Persinger MA, Parker GH (1994) Prevention of sudden cardiac death by the atypical neuroleptic acepromazine following status epilepticus in rats. *Life Sci* 54:457–462
- Leestma JE, Walczak T, Hughes JR, Kalekar MB, Teas SS (1989) A prospective study on sudden unexpected death in epilepsy. *Ann Neurol* 26:195–203
- Lerchl A, Reiter RJ, Howes KA, Nonaka KO, Stokkan K-A (1991) Evidence of extremely low frequency Ca^{++} resonance depresses pineal melatonin synthesis in vitro. *Neurosci Lett* 1991:213–215
- Mayaud PN (1975) Analysis of storm sudden commencements for the years 1868–1967. *J Geophys Res* 80:111–121
- Mevissen M, Ebert U (1998) Anticonvulsant effects of melatonin in amygdala-kindled rats. *Neurosci Lett* 257:13–16
- Michon AL, Persinger MA (1997) Experimental simulation of the effects of increased geomagnetic activity upon nocturnal seizures in epileptic rats. *Neurosci Lett* 224:53–56
- Myers B, Badia P (1993) Factors affecting endogenous melatonin levels. *Sleep Res* 22:2
- O'Connor RP, Persinger MA (1997) Geophysical variables and behavior LXXXII: a strong association between sudden infant death syndrome (SIDs) and increments of global geomagnetic activity-possible support for the melatonin hypothesis. *Percept Mot Skills* 84:395–402
- Oppenheimer SM, Wilson JX, Guiraudon C, Cechetto DF (1991) Insular cortex stimulation produces lethal cardiac arrhythmias: a mechanism of sudden death? *Brain Res* 550:115–121
- Persinger MA (1995a) Sudden unexpected death in epileptics following sudden, intense, increases in geomagnetic activity: prevalence of affect and potential mechanisms. *Int J Biometeorol* 38:180–187
- Persinger MA (1995b) Geophysical variables and behavior: LXXIX. Overt limbic seizures are associated with concurrent and pre-midscotophase geomagnetic activity: Synchronization by prenocturnal feeding. *Percept Mot Skills* 81:83–93
- Persinger MA (1996) Enhancement of limbic seizures by nocturnal application of experimental magnetic fields that simulate the magnitude and morphology of increases in geomagnetic activity. *Int J Neurosci* 86:271–280
- Persinger MA (2003) Neurobehavioral effects of brief exposures to weak intensity, complex magnetic fields within experimental and clinical settings. In: McLean MU, Engstrom S, Holcomb RR (eds) *Magnetotherapy: therapeutic benefits and adverse effects*. TFG, New York, pp 89–115
- Persinger MA, Belanger-Chellew G (1999) Facilitation of seizures in limbic epileptic rats by complex 1 microTesla magnetic fields. *Percept Mot Skills* 89:486–492
- Persinger MA, Bureau YRJ, Kostakos M, Peredery O, Falter H (1993) Behaviors of rats with insidious multifocal brain damage induced by seizures following single peripheral injections of lithium and pilocarpine. *Physiol Behav* 53:849–866
- Racine RJ (1972) Modification of seizure activity by electrical stimulation II. Motor seizure. *Electroencephalogr Clin Neurophysiol* 32:281–284
- Rajaram M, Mitra S (1981) Correlation between convulsive seizure and geomagnetic activity. *Neurosci Lett* 24:187–191
- Reiter RJ (1993) Static and extremely low frequency electromagnetic field exposure: reported effects on the circadian production of melatonin. *J Cell Biochem* 51:393–403
- Schnabel R, Beblo M, May TW (2000) Is geomagnetic activity a risk factor for sudden unexplained death in epilepsies? *Neurology* 54:903–908
- Schapel GJ, Beran RG, Kennaway DL, McLoughney J, Matthews CD (1995) Melatonin response in active epilepsy. *Epilepsia* 36:75–78
- Stewart LS, Persinger MA (2001) Ketamine prevents learning impairment when administered immediately after status epilepticus onset. *Epilepsy Behav* 2:585–591
- Stoupel E, Domarkiene S, Radishauskas R, Abramson E (2002) Sudden cardiac death and geomagnetic activity: links to age, gender and agony time. *J Bas Clin Physiol Pharmacol* 13:11–21
- Terrance CF (1990) Unexpected, unexplained death of epileptic persons: clinical correlation including pulmonary changes. In: Lathers CM, Schraeder PL (eds) *Epilepsy and sudden death*. Dekker, New York, pp 89–100
- Yaga K, Reiter RJ, Manchester LC, Nieves H, Sun J-H, Chen L-D (1993) Pineal sensitivity to pulsed static magnetic field changes during the photoperiod. *Brain Res Bull* 30:153–156
- Zeiss ML, Semm P (1988) Melatonin lowers excitability of guinea pig hippocampal neurons in vitro. *J Comp Physiol A* 157:23–29